

## **REMARKS**

### **I. Background**

The present amendment and remarks are in response to the Office Action mailed February 3, 2009. Applicant has amended claims 13, 16-22, 24, and 34. Applicant has cancelled claim 14. New claim 35 has been added. As such, claims 13, 15-26 and 29-35 are currently pending for consideration on the merits.

Reconsideration of the claims is respectfully requested in view of the above amendments to the claims and the following remarks. For the Examiner's convenience and reference, Applicant's remarks are presented in the order in which the corresponding issues were raised in the Office Action.

Please note that the following remarks are not intended to be an exhaustive enumeration of the distinctions between any cited reference and the claimed invention. Rather, the distinctions identified and discussed below are presented solely by way of example to illustrate some of the differences between the claimed invention and the cited references. In addition, Applicant requests that the Examiner carefully review any reference discussed below to ensure that Applicant's understanding and discussion of the references, if any, is consistent with the Examiner's understanding.

### **II. Rejection on the Merits**

#### **A. 35 USC § 112 Second Paragraph**

The Office Action rejects claims 13-26 and 29-34 under 35 USC § 112, second paragraph, as being indefinite for omitting essential steps, such omission amounting to a gap between the steps. Applicant respectfully asserts that Zhang does not teach the presently claimed method steps and does not produce stratified, terminally-differentiated human urothelial cells as presently claimed. Additionally, the Declarations of Jennifer Southgate, Ph.D. and William Cross, Ph.D. are being filed herewith to provide evidence that Zhang does not teach the presently claimed invention. Applicant submits that the claimed method is substantially and patentably distinct from *Zhang et al* (In vitro Cell. Dev. Biol.-Animal 2001). As such, the Zhang reference cannot be construed in a manner so show the presently claimed invention is missing an essential

method step or component.

Additionally, claims 17, 18, and 34 were rejected for various typographical errors, which have not been corrected.

In view of the foregoing, Applicant respectfully requests withdrawal of the rejection under 35 USC § 112, first paragraph.

**B. 35 USC § 102(b)**

The Office Action rejects claims 13, 15, 17-19, 23-26, and 29-34 under 35 USC § 102(b) as being anticipated by the article by *Zhang et al* (In vitro Cell. Dev. Biol.-Animal 2001). Applicant respectfully traverses the rejection because the Office Action has not established that *Zhang* teaches each and every claim element in the presently pending claims.

In accordance with Applicant's understanding, *Zhang* discloses the cultivation of rat urothelial cells (RUC) in a range of growth media, including a conditioned medium "KSFM-CM".

Accordingly, Applicant respectfully asserts that *Zhang* does not teach each and every element of the presently claimed invention recited in claims 13, 24, and 34. More particularly, *Zhang* is completely devoid of teaching or suggesting a "method of production of stratified, terminally-differentiated human urothelium." *Zhang*, however, only teaches about rat urothelium. Thus, *Zhang* does not teach each and every element of the presently claimed invention recited in claims 13, 24, and 34. Since *Zhang* does not teach each and every claim element, *Zhang* does not anticipate the presently claimed invention recited in claims 13 and 24. Since claims 13, 15, 17-19, 21-26, and 29-34 depend from claims 13 or 24, such claims include the same claim elements and are allowable for at least the same reasons that claims 13 and 24 are allowable. Thus, Applicant respectfully requests withdrawal of the rejection under 35 U.S.C. § 102(e) with respect to *Zhang*.

The Office Action rejects claims 13, 15, and 23 under 35 USC § 102(b) as being anticipated by the article by *Liebert et al.* (Differentiation 1997). Applicant respectfully traverses the rejection because the Office Action has not established that *Liebert* teaches each and every claim element in the presently pending claims. However, claim 14 has not been rejected as being anticipated by *Liebert*. Applicants agree, and have amended claim 13 to

include the elements of claim 14. Thus, *Liebert* does not teach each and every element of the presently claimed invention recited in claim 13.

Since *Liebert* does not teach each and every claim element, *Liebert* does not anticipate the presently claimed invention recited in claim 13. Since claims 15 and 23 depend from claim 13, such claims include the same claim elements and are allowable for at least the same reasons that claim 13 is allowable. Thus, Applicant respectfully requests withdrawal of the rejection under 35 U.S.C. § 102(e) with respect to *Liebert*.

#### C. 35 USC § 103

The Office Action rejects claim 16 under 35 USC § 103(a) as being obvious over the articles by *Zhang* or *Liebert* in view of *Sejiro et al.* (U.S. Patent No. 4,654,304). Applicant respectfully asserts that the Office Action has not established a *prima facie* case of obviousness because the proposed combination of references (e.g., *Zhang*, *Liebert*, and *Sejiro*) does not teach or suggest each and every element of the presently claimed invention.

In accordance with Applicant's understanding, *Sejiro* only teaches or suggests cell culture compositions that promote cell growth, but not cell differentiation. In fact, *Sejiro* does not teach a cell culture media that promotes cell differentiation. Cell growth is an entirely different process from cell differentiation. Thus, *Sejiro* does not teach the use of adult bovine serum for cell differentiation, and a skilled artisan would not consult *Sejiro* in preparing a cell culture media that promotes cell differentiation.

The foregoing discussions of *Zhang* and/or *Liebert* are applicable to this rejection, and are hereby incorporated into this remark by specific reference. Applicant respectfully asserts that *Sejiro* does not cure the deficiencies of *Zhang* and/or *Liebert*, which were discussed above. Applicant asserts that the combination of *Zhang* and *Liebert* with *Sejiro* does not teach or suggest a "method of production of stratified, terminally-differentiated human urothelium in which urothelial cells, isolated from the human body and propagated by culture in serum-free medium, are transferred to a first nutrient differentiation medium containing serum and then redispersed by passage before being added to a second nutrient differentiation medium containing serum to form said urothelium, wherein the first nutrient differentiation medium is not the second nutrient differentiation medium," as recited in claim 13. Since the combination of

references (e.g., *Zhang*, *Liebert*, and *Sejiro*) does not teach or suggest each and every element of the presently claimed invention, a *prima facie* case of obviousness has not been established with respect to claim 13. Since claim 16 depends from claim 13, claim 16 includes the same claim elements and is allowable for at least the same reasons claim 13 is allowable. Thus, Applicant respectfully requests withdrawal of the rejection of claim 16 under 35 U.S.C. § 103(a).

The Office Action rejects claims 20 and 22 under 35 USC § 103(a) as being obvious over *Zhang* in view of *Judd et al.* (U.S. Patent No. 6,692,961). Applicant respectfully asserts that the Office Action has not established a *prima facie* case of obviousness because the proposed combination of *Zhang* and *Judd* does not teach or suggest each and every element of the presently claimed invention.

In accordance with Applicant's understanding, *Judd* teaches the development of defined growth media (i.e. not containing serum) for the propagation of epithelial cells, but does not teach the defined media can be used for human urothelial cell differentiation. As stated above, cell growth is an entirely different process from human urothelial cell differentiation, and cell differentiation has different media requirements. Thus, *Judd* does not teach the use of a defined medium for cell differentiation, and a skilled artisan would not consult *Judd* in preparing a cell culture media that promotes human urothelial cell differentiation.

The foregoing discussion of *Zhang* is applicable to this rejection, and is hereby incorporated into this remark by specific reference. Applicant respectfully asserts that *Judd* does not cure the deficiencies of *Zhang*. That is, *Judd* does not teach the claim limitations of claim 13, and the combination of *Zhang* and *Judd* is completely devoid of teaching or suggesting a "method of production of stratified, terminally-differentiated human urothelium in which urothelial cells, isolated from the human body and propagated by culture in serum-free medium, are transferred to a first nutrient differentiation medium containing serum and then redispersed by passage before being added to a second nutrient differentiation medium containing serum to form said urothelium, wherein the first nutrient differentiation medium is not the second nutrient differentiation medium," as recited in claim 13. Since the combination of *Zhang* and *Judd* does not teach or suggest each and every element of the presently claimed invention, a *prima facie* case of obviousness has not been established with regard to claim 13. Since claim 20 depends from claim 13, claim 20 includes the same claim elements and is allowable for at least the same

reasons claim 13 is allowable. Thus, Applicant respectfully requests withdrawal of the rejection of claim 20 under 35 U.S.C. § 103(a).

The Office Action rejects claims 20 and 22 under 35 USC § 103(a) as being obvious over *Liebert* in view of *Judd*. Applicant respectfully asserts that the Office Action has not established a *prima facie* case of obviousness because the proposed combination of *Liebert* and *Judd* does not teach or suggest each and every element of the presently claimed invention.

The foregoing discussions of *Liebert* and *Judd* are applicable to this rejection, and are hereby incorporated into this remark by specific reference. Applicant respectfully asserts that *Judd* does not cure the deficiencies of *Liebert*. That is, *Judd* does not teach the claim limitations of claim 13, and the combination of *Liebert* and *Judd* is completely devoid of teaching or suggesting a “method of production of stratified, terminally-differentiated human urothelium in which urothelial cells, isolated from the mammalian body, are passaged through a first nutrient medium containing serum and then redispersed before being added to a second medium containing serum to form said urothelium,” as recited in claim 13.

Since the combination of *Liebert* and *Judd* does not teach or suggest each and every element of the presently claimed invention, a *prima facie* case of obviousness has not been established with regard to claim 13. Since claims 20 and 22 depend from claim 13, claims 20 and 22 each include the same claim elements and is allowable for the same reasons claim 13 is allowable. Thus, Applicant respectfully requests withdrawal of the rejection of claims 20 and 22 under 35 U.S.C. § 103(a).

The Office Action rejects claims 13-15 and 17-19, 21, 23-34 under 35 USC § 103(a) as being obvious over the *Cross et al.* (Biochemical Society Transactions 2001) in view of *Zhang*. Applicant respectfully asserts that the Office Action has not established a *prima facie* case of obviousness because the proposed combination of references (e.g., *Cross* in view of *Zhang*) does not teach or suggest each and every element of the presently claimed invention.

Applicants understandings of the combination of *Zhang* and *Cross* is provided in the attached Declaration of Jennifer Southgate, Ph.D. and William Cross, Ph.D. under 37 CFR 1.132 (hereinafter “Southgate and Cross Declaration”). The Declaration of David John Tweats, Ph.D. (hereinafter “Tweats Declaration) is also attached to provide evidence of the knowledge and understanding of the art from an unbiased expert. Applicant asserts, with support from the

declarations, that the combination of *Zhang* and *Cross* does not teach or suggest a “method of production of stratified, terminally-differentiated human urothelium in which urothelial cells, isolated from the human body and propagated by culture in serum-free medium, are transferred to a first nutrient differentiation medium containing serum and then redispersed by passage before being added to a second nutrient differentiation medium containing serum to form said urothelium, wherein the first nutrient differentiation medium is not the second nutrient differentiation medium,” as recited in claim 13. Similarly, the combination of *Zhang* and *Cross* is also completely devoid of teaching or suggesting the methods of claims 24 and 34. Thus, the combination of *Zhang* and *Cross* does not teach or suggest each and every claim element of the claims 13, 24, and 34.

Additionally, both the Southgate and Cross Declaration and Tweats Declaration provide evidence of secondary considerations that rebut the alleged obviousness. The secondary considerations are (1) a long-felt need in the art for the present invention, (2) the failure of others, and (3) the surprising and unexpected results obtained by the inventors when practicing the presently claimed invention.

Since the combination of *Zhang* and *Cross* does not teach or suggest each and every element of the presently claimed invention and the presence of significant secondary considerations, a *prima facie* case of obviousness has not been established with respect to claims 13-15 and 17-19, 21, 23-33. Thus, Applicant respectfully requests withdrawal of the rejection of claim 13-15, 17-26, and 29-32 under 35 U.S.C. § 103(a).

### **III. References Teach Away From Claims**

Applicant respectfully asserts that the art of record recited in the rejections discussed above teach away from the presently claimed invention. In part, this is because the presently claimed invention recites that human urothelial cells grown in a serum-containing media are redispersed into another serum-containing medium. However, none of the art of record teaches such redispersal from a serum-containing medium into another serum-containing medium. After a reading of the art of record, the skilled artisan would not be motivated to redisperse human urothelial cells from a serum-containing medium into another serum-containing medium because

redispersal of such cells constitutes an action that is apparently diametrically opposed to achieving the desired result of an organized, stratified, terminally-differentiated human urothelium. Accordingly, the skilled artisan would seek to maintain any structure from the first culture stage, rather than disrupting it by redispersal, and would have no motivation to overturn this technical prejudice.

### **CONCLUSION**

In view of the foregoing, Applicant respectfully submits that the other rejections to the claims are now moot and do not, therefore, need to be addressed individually at this time. It will be appreciated, however, that this should not be construed as Applicant acquiescing to any of the purported teachings or assertions made regarding the cited art or the pending application, including any Official Notice. Instead, Applicant reserves the right to challenge any of the purported teachings or assertions made in any action at any appropriate time in the future, should the need arise. Furthermore, to the extent that the Examiner has relied on any Official Notice, explicitly or implicitly, Applicant specifically requests that the Examiner provide references supporting the teachings officially noticed, as well as the required motivation or suggestion to combine the relied upon Notice with the other art of record.

Applicant believes claims 13, 15-26 and 29-35 are in allowable form as discussed above. As such, Applicant respectfully requests reconsideration of the application and allowance of presently pending claims. In the event that the Examiner finds remaining impediment to a prompt allowance of this application that may be clarified through a telephone interview, the Examiner is requested to contact the undersigned attorney by telephone at (801) 533-9800.

Dated this 29<sup>th</sup> day of October 2009.

Respectfully submitted,

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